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EXAMINER	
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ART UNIT	PAPER NUMBER
1631	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/660,110	OLDHAM ET AL.	
	Examiner	Art Unit	
	Russell S. Negin	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20,23-34 and 36-55* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20,23-34 and 36-55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Comments

Applicants' request for reconsideration in the communication filed on 2 November 2007 is acknowledged and the amendments are entered.

Claims 20, 23-34, and 36-55 are pending and examined in the instant Office action.

Withdrawn Objections/Rejections

The objection to claim 23 is withdrawn due to amendments filed by applicant to the instant claim on 2 November 2007.

The rejections of claims 20-44 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention are withdrawn in view of amendments filed to the set of claims on 2 November 2007.

The rejection of claim 20 under 35 U.S.C. 103(a) as being unpatentable over Tomlinson et al. [Electrophoresis, 1994, volume 15, pages 62-71] in view of Likuski [US Patent 5,932,080 issued 3 August 1999] is withdrawn in view of amendments made to the claim on 2 November 2007.

The following rejections are newly applied:

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 20, 23-32 and 47-55 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 20 recites the limitation "the first and second parameters" in line 23.

Claim 45 recites the limitation "the first and second parameters" in line 20.

There is insufficient antecedent basis for this limitation in claims 20 and/or 45. The term "parameter" is not previously recited previously in either of the claims. For the purposes of examination, it will be assumed that such "parameters" are the intensities of the respective signals.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 20, 23, and 45-46 are rejected under 35 U.S.C. 102(b) as being anticipated by Kobayashi et al. [Journal of Chromatography, volume 480, 1989, pages 179-184].

Claims 20 and 45 are drawn to a method for improving the measurement of a plurality of types of specific particles of a sample using a photodetector associated with a biological analysis system wherein the specific particles are adapted to emit identifiable signals based on the interaction of the specific particles with corresponding probes and wherein the identifiable signals are captured by the photodetector to yield an output signal and wherein the photodetector is adapted to be operated at different configurations that respond differently to the identifiable signals, the method comprising:

--performing a first measurement of the identifiable signals with the photodetector at a first configuration such that the photodetector yields a first output signal representing a measurement of a first type of the plurality of types of specific particles, wherein the first measurement at the first configuration is adapted to measure a first component of the identifiable signals;

--performing a second measurement of the identifiable signals with the photodetector at a second configuration such that the photodetector yields a second output signal representing a measurement of a second type of the plurality of specific particles, wherein the second measurement at he second configuration is adapted to measure a second component of the identifiable signals, the second component is weaker that the first component, and the particles of the first type of specific particles

are more abundant in the sample than the particles of the second type of specific particles; and

--adjusting one of the first and second output signals based on a relationship between the first and second parameters to obtain a separately scaled representation of at least one of the identifiable signals wherein the representation of the identifiable signals includes generating representations of the first and second types of the plurality of types of specific particles.

Claim 45 is drawn to similar subject matter, except instead of the second component being weaker than the first component, the second component is stronger than the first component.

The study of Kobayashi et al. teaches a photodiode array detection system for high performance capillary electrophoresis. Figure 7 on page 183 of Kobayashi et al. shows an electropherogram of a plurality (i.e. six) types of particles. The electropherogram is a profile of the electrically induced flow of the constituents of the mixture as a function of time through a capillary as observed by a photodetector at the end of the capillary (i.e. see Figure 1 on page 180 of Kobayashi et al. for the configuration).

Since the photodetector in the CE apparatus is a photodiode array detector, its configuration is adapted to perform the measurements of the particles at multiple wavelengths. For example, Figure 8 of Kobayashi et al. shows the extended absorption

curves at 218 and 326 nm for component 1 and 200, 209, and 276 nm for components 2 and 3.

In applying the prior art to instant claim 20, the first configuration and first type of particle is interpreted to be 0.81 mM nicotinamide (i.e. peak 1) measured in Figure 8A of Kobayashi et al. at 326 nm (the first configuration of the detector). Additionally, the second configuration and second type of particle in interpreted to be 0.52 mM caffeine (i.e. peak 2) measured in Figure 8B of Kobayashi et al. at 200 nm (the second configuration of the detector). The abundance of the nicotinamide (the first type of particle) is greater than that of the caffeine (the second type of particle- see page 180 of Kobayashi et al. for the concentrations of each of the species in the mixtures). Furthermore, the intensity of the nicotinamide signal is greater than that of the caffeine signal.

The representations of the signal intensities in Figures 8A and 8B are scaled (i.e. adjusted) so their representations are equally observable when placed side-by side.

Consequently, the configuration of the photodiode arrays detector is adapted by adjusting the observable wavelength to respond differently to the identifiable signals. For instant claim 45, the above claim analysis should be repeated by reversing the particle types 1 and 2.

Claims 23 and 46 are further limiting wherein adjusting one of the first and second output signals comprises scaling the first output signal to a scale associated with second configuration such that, based on the second configuration, the second

component is measured and the first component is represented based on the scaling of the measured value from the first configuration.

As stated above, the representations of the signal intensities in Figures 8A and 8B are scaled (i.e. adjusted) so their representations are equally observable when placed side-by side; consequently, the scaling of the intensities each of the signals are based on the scaling of the other signal (i.e. the scaling of the second component is based on the scaling of the first component).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

35 U.S.C. 103 Rejection #1:

Claims 24, 33-34, 36, and 47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kobayashi et al. as applied to claims 20, 23, and 45-46 above, and further in view of Tomlinson et al. [Electrophoresis, 1994, volume 15, pages 62-71]

Claim 33 is drawn to a method of extending the dynamic range of a photodetector that measures detectable signals from a sample undergoing a biological analysis where the detectable signals represent two or more components of the sample, the method comprising:

--obtaining a first output signal form the photodetector operated at a first configuration that allows measurement of a first component of the detectable signals;

--obtaining a second output signal from the photodetector operated at a second configuration that allows measurement of a second component of the detectable signals wherein the second configuration is such that the first component of the detectable signals would fall outside the photodetector's dynamic range; and

--scaling separately the first output signal to a scale associated with the second configuration wherein the amount of scaling depends on the first and second configurations and wherein the separately scaled first output signal allows the generation of a representation of the first output signal at the second configuration.

Claim 34 is further limiting wherein the first component of the detectable signals is stronger that the second component of the detectable signals.

Claims 24, 36, and 47 are further limiting wherein the scaling of the first component allows representation of both the second and first components when a dynamic range associated with the detector is limited and would not be able to measure the first component at the second configuration.

Kobayashi et al. teaches a photodiode array detector that measures a plurality of different particle types at a plurality of different configurations (i.e. wavelengths).

Kobayashi et al. does not teach extending the dynamic range of the detector.

Tomlinson et al. teaches the differences and advantages of using capillary electrophoresis equipped with photodiode array detection over conventional CE with UV detection for the purpose of drug analysis. One of the advantages is that CE equipped with photodiode array detection extends the dynamic range of detecting particle signals. For example, the absorbance intensity scales on the ordinate axes in the electropherograms of haloperidol (HAL) in Figure 4 (CE-DAD; page 66 of Tomlinson et al.) is an order of magnitude greater than the HAL in Figure 3 (CE, page 66 of Tomlinson et al.) Using photodiode array detection, consequently, increases the absorbance intensities and dynamic range of the photodetector over conventional CE. Additionally, photodiode array detectors allow for a complete UV spectrum as a function of time for an analyte [see first paragraph, column 2 of page 66 of Tomlinson et al.]

It would have been obvious for someone of ordinary skill in the art at the time of the instant invention to modify the photodiode array detection system of Kobayashi et al.

by use of the investigation of drug metabolism using photodiode array detectors of Tomlinson et al. where the motivation would have been that the increased intensities and variable wavelengths of CE-DAD allow for analysis of more complex drug containing mixtures in a manner that is more efficient [see first paragraph, column 2 of page 66 of Tomlinson et al.]

35 U.S.C. 103 Rejection #2:

Claims 28-29, 31-32, 40-41, 43-44, 51-52, and 54-55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kobayashi et al. in view of Tomlinson et al. as applied to claims 20, 23, 24, 33, 34, 36, and 45-47 above, and further in view of Photomultiplier Tubes [Hamamatsu Brochure, pages 1-15, July 2002].

Claims 28, 40, and 51 are further limiting wherein the detector is a charge multiplier and the first configuration comprises an operating voltage V1 selected to measure the first component of the identifiable signals.

Claims 29, 41, and 52 are further limiting wherein the second configuration comprised an operating voltage V2 selected to measure the second component of the identifiable signals, wherein the operating voltage V2 is higher (or lower for claim 52) than the operating voltage V1.

Claims 31, 43, and 54 are further limiting wherein the charge multiplier comprises photomultiplier tubes.

Claims 32, 44, and 55 are further limiting wherein the charge multiplier comprises a charge intensifier.

The studies of Kobayashi et al. and Tomlinson et al. make obvious drug metabolism using capillary electrophoresis with photodiode array detection, as discussed above.

Tomlinson et al. discloses two separate voltages for the two separate configurations disclosed in Figures 3 and 4; one configuration uses a voltage of 20kV, the second uses a voltage of 30 kV- a voltage greater than in the first configuration. (For claim 52, the configurations are interpreted to be reversed).

However, Kobayashi et al. and Tomlinson et al. do not disclose charge multipliers, specifically, in the forms of photomultiplier tubes and charge intensifiers.

The catalog "Photomultiplier tubes" discusses uses and sales of photomultiplier tubes and charge intensifiers throughout the brochure.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the photodetector studies of Kobayashi et al. and Tomlinson et al. by use of the photomultiplier tubes and charge intensifiers of the Hamamatsu Brochure because it would have been obvious to apply a known technique to a known method to yield a predictable result. In this instance, it would have been obvious to apply the techniques of using photomultipliers and charge intensifiers to the methods of signal analysis of Kobayashi et al. and Tomlinson et al. to result in modified electropherogram absorbance intensities. There would have been a reasonable expectation of success in incorporating the photomultiplier tubes into the detectors of Kobayashi et al. and Tomlinson et al. because such photomultiplier tubes and charge multipliers provide an alternative means for measuring the intensities of particles in a

mixture (i.e. a photomultiplier detects photons and converts them into electropherograms or electrical signals).

35 U.S.C. 103 Rejection #3:

Claims 30, 42, and 53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kobayashi et al. in view of Tomlinson et al. in view of Photomultiplier tubes as applied to claims 20, 23-24, 28-29, 31-34, 36, 40-41, 43-47, 51-52, and 54-55 above, in further view of Priebe [19th Annual Symposium of Frequency Control, 1965, pages 487-508].

Claims 30, 42, and 53 are further limiting wherein the scaling of the first output signal comprises determining the scaled value N1 of the first output signal based on a relationship log (N1) = m log (V2/V1) wherein m represents a slope of a curve obtained by plotting the multiplier's gain versus the voltage in a log-log manner.

The studies of Kobayashi et al., Tomlinson et al. and the Photomultiplier Tube brochure investigates drug metabolism using capillary electrophoresis with photodiode array detection, as discussed above.

Kobayashi et al., Tomlinson et al. and the Photomultiplier tube brochure do not discuss the specific relation in the instant set of claims.

The study of Priebe investigates the attenuation and resistance measurements of unwanted modes of quartz crystals.

Specifically, equation 2 of Priebe shows that the attenuation of the signal from the crystal (in Decibel) is proportional to the logarithm of the ratios of two voltages with the proportionality constant (m) being 20.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the photodetector measurements using photomultiplier tubes of Kobayashi et al., Tomlinson et al. and Hamamatsu (i.e. Brochure) by further use of the relation of Priebe because it would have been obvious to apply a known technique to a known method to yield a predictable result. In this instance, it would have been obvious to apply the known signal attenuation techniques of Priebe to the photodetector system of Kobayashi et al., Tomlinson et al. and Hamamatsu to yield the predictable outcome of comparably attenuated signals. There would have a reasonable expectation of success in combining the relations of Priebe with photomultiplers tubes and photodiode array detectors of Kobayashi et al. and Tomlinson et al. because the relation of Priebe allows for the attenuation of a multiplier's gain.

35 U.S.C. 103 Rejection #4:

Claims 25-26, 37-38, and 48-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kobayashi et al. in view of Tomlinson et al. as applied to claims 20, 23, 24, 33, 34, 36, and 45-47 above, and further in view of Tacklind et al [US PGPUB 2003/0101605; issued 5 June 2003; filed 4 December 2001].

Claims 25, 37, and 48 are further limiting wherein the detector is a charge-coupled device and the first configuration comprises an exposure duration T1 selected to measure the first component of the identifiable signals.

Claims 26, 38, and 49 are further limiting wherein the second configuration comprises an exposure duration T2 selected to measure the second component of the identifiable signals, wherein the exposure duration T2 is longer (or shorter for claim 49) than the exposure duration T1.

The studies of Kobayashi et al. and Tomlinson et al. investigate drug metabolism using capillary electrophoresis with photodiode array detection, as discussed above.

Tomlinson et al. plots two separate migration times for the two separate configurations, with one set (i.e. CE-DAD or Figure 4) having a greater length in migration time (T2) than solely CE (CE is Figure 3, or T1). Depending on which of claims 48-49 are being analyzed, the configuration assignments could be reversed so that T2 is shorter in duration that T1.

However, Kobayashi et al and Tomlinson et al. do not disclose a charge multiplier.

The invention of Tacklind et al. studies servo-controlled automatic level and plumb tool and explains the use of charge coupled devices in paragraph [0060] where it is stated that "The position sensitive photo sensor can incorporate any of a number of commercially available position sensitive detectors sensitive to the detector light... Examples include charged coupled detectors (CCD)."

Consequently, charged coupled detectors are used to assist in analyzing signals from detectors.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the photodetector analyses of Kobayashi et al. and Tomlinson et al. by use of the CCDs of Tacklind et al. because it is obvious to apply a known technique to a known method to yield a predictable result. In this instance, it would have been obvious to apply the known technique of using CCDs to analyze signals to the known method of comparing CE and CE-DAD spectra of Kobayashi et al. and Tomlinson et al. to yield the predictable result of modified spectra and a modified means of receiving the relevant signals. There would have been a reasonable expectation of success in combining a CCD of Tacklind et al. with the CE and CE-DAD of Kobayashi et al. and Tacklind et al. because the charge coupled device of Tacklind et al. allows an alternative means of measuring the intensities of particles and converting them into electrical signals.

35 U.S.C. 103 Rejection #5:

Claims 27, 39, and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kobayashi et al. in view of Tomlinson et al. in view of Tacklind et al. as applied to claims 20, 23-26, 33, 34, 36-38, and 45-49 above, and further in view of Pierre et al. [IEEE Acoustics, Speech, and Signal Processing. 1995, pages 1900-1903].

Claims 27, 39 and 50 are further limiting wherein the scaling of the first output signal comprises multiplying the first output signal value by a ratio of T2/T1.

The study of Kobayashi et al., Tomlinson et al. and Tacklind et al. make obvious drug metabolism using capillary electrophoresis with photodiode array detection using CCDs, as discussed above.

While Tomlinson et al. teaches two separate migration times, Kobayashi et al., Tomlinson et al. and Tacklind et al. do not teach multiplying the signal by a ratio of T2/T1.

The article of Pierre et al. studies the consideration in the autocalibration of quadrature receivers in which Figure 2 on page 1902 of Pierre et al. illustrates a log-log plot of the variance of the signal to noise ratio as a function of the ratio of two times. The purpose of the simulation plotted in Figure 2 of Pierre is to illustrate the variance in signal to noise ratio as observation time increases.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the photodetector analysis of CE using CCDs of Kobayashi et al., Tomlinson et al. and Tacklind et al. by use of the time ratio simulation of Pierre et al. where the motivation would have been that Pierre et al. gives information regarding signal accuracy (in terms of variance in signal to noise ratio) as a function of observance time [see page 1903 of Pierre et al.]

Conclusion

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the

central PTO Fax Center. The faxing of such pages must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)). The Central PTO Fax Center Number is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Negin, Ph.D., whose telephone number is (571) 272-1083. The examiner can normally be reached on Monday-Friday from 7am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisor, Marjorie Moran, Supervisory Patent Examiner, can be reached at (571) 272-0720.

Information regarding the status of the application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information on the PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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21 January 2008

/Marjorie A. Moran/
SPE, AU 1631
1/22/2008